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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/494,585	01/31/2000	Richard A. Shimkets	15966-557(Cura-57)	3648

7590 09/17/2002

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EXAMINER	
SAOUD, CHRISTINE J	

ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 09/17/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/494,585	Applicant(s) SHIMKETS et al.
	Examiner Christine Saoud	Art Unit 1647

-- *The MAILING DATE of this communication appears on the cover sheet with the correspondence address* --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) [X] Responsive to communication(s) filed on *Jun 28, 2002*.

2a) [X] This action is **FINAL**. 2b) [ ] This action is non-final.

3) [ ] Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) [X] Claim(s) *1, 2, 4, 7-10, 14, 19-21, 28, and 29* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) [ ] Claim(s) _____ is/are allowed.

6) [X] Claim(s) *1, 2, 4, 7-10, 14, 19-21, 28, and 29* is/are rejected.

7) [ ] Claim(s) _____ is/are objected to.

8) [ ] Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) [X] The specification is objected to by the Examiner.

10) [ ] The drawing(s) filed on _____ is/are a) [ ] accepted or b) [ ] objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) [ ] The proposed drawing correction filed on _____ is: a) [ ] approved b) [ ] disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) [ ] The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) [ ] Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) [ ] All b) [ ] Some* c) [ ] None of:

1. [ ] Certified copies of the priority documents have been received.
2. [ ] Certified copies of the priority documents have been received in Application No. _____.
3. [ ] Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) [X] Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) [ ] The translation of the foreign language provisional application has been received.

15) [ ] Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) [ ] Notice of References Cited (PTO-892)
2) [ ] Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) [X] Information Disclosure Statement(s) (PTO-1449) Paper No(s). *16*
4) [ ] Interview Summary (PTO-413) Paper No(s). _____
5) [ ] Notice of Informal Patent Application (PTO-152)
6) [ ] Other:

DETAILED ACTION

Response to Amendment

1. Claims 3 and 6 have been canceled, claims 1, 5, 14, 19, 20, 28 and 29 have been amended as requested in the amendment of paper #15, filed 28 June 2002. Claims 1-2, 4-5, 7-10, 14, 19-21 and 28-29 are pending in the instant application. Applicant requested that claim 21 be withdrawn from consideration as being directed to a non-elected invention (see page 2 of paper #15). Accordingly, claims 1-2, 4-5, 7-10, 14, 19-20 and 28-29 are under examination in the instant application. Claim 21 is still pending, but is withdrawn as requested by Applicant.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

3. Any objection or rejection of record which is not expressly repeated in this action has been overcome by Applicant's response and withdrawn.

4. Applicant's arguments filed 28 June 2002 have been fully considered but they are not deemed to be persuasive.

It is noted that claim 14 was inadvertently omitted from the 101/112 rejection of the claims. However, it is clear that this was a typographical error since the subject matter of claim 14 is a method of making the protein using a host cell comprising the DNA encoding the protein.

The DNA and host cell were rejected for lack of utility since the protein had no utility. Therefore, the reasonably follows that the method of making the protein also has no utility if the protein and encoding DNA have no utility. Since Applicant's arguments regarding claims 1-10, 19-21 and 28-29 fairly address the rejection that should have included claim 14, the correction of the rejection to include claim 14 does not raise any new issues or grounds of rejection and the instant action can be properly made final.

Specification

5. The abstract of the disclosure is still objected to because it refers to speculative applications of the invention. Correction is required. Failure to correct the abstract to remove the speculative applications (i.e. use for detection and treatment of pathological states) will be considered non-responsive. See MPEP § 608.01(b).

Claim Objections

6. Claim 2 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claim 2 is duplicative of claim 1, absent evidence to the contrary.

Claim Rejections - 35 USC § 101

7. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

8. Claims 1-2, 4-5, 7-10, 14, 19-20, 28-29 are rejected under 35 U.S.C. 101 because the claimed invention is drawn to an invention with no apparent or disclosed specific and substantial credible utility for the reasons of record in paper #12.

9. The Declaration under 37 CFR 1.132 filed 28 June 2002 is insufficient to overcome the rejection of claims 1-2, 4-5, 7-10, 14, 19-20, 28-29 based upon lack of utility as set forth in the last Office action because: the ability of the disclosed protein to stimulate and transform NIH 3T3 cells in culture does not provide a specific, substantial and credible utility for the claimed invention. The disclosed protein would not be useful for stimulating fibroblast cells if it also induces their transformation and likewise, just because it transforms fibroblast cells in culture does not indicate that it is involved in cancer. Applicant asserts that because the disclosed protein stimulates cell growth and proliferation, it would therefore be involved in many human proliferation-associated disorders. This argument is not persuasive. A number of different proteins may be found to have activity in culture, but these proteins fail to play any role in the normal development and progression of diseases *in vivo*. The specification asserts that the "FGF-CX" protein of the instant application could be used in a method of diagnosing a tissue proliferation-associated disorder, "such as tumors, restenosis, psoriasis, diabetic and post-surgery complications, and rheumatoid arthritis" (see page 4, lines 26-28 of the specification), in a method of "treating or preventing or delaying a tissue proliferation-associated disorder" (page 5, lines 28-29 of the specification) by administration of a FGF-CX nucleic acid, polypeptide or antibody.

wherein the disorder includes tumors, restenosis, psoriasis, Dupuytren's contracture, diabetic complications, Kaposi sarcoma, and rheumatoid arthritis (see page 6, lines 6-7 of the specification), in a method of treating or diagnosing glia-associated disorders, including "cerebral lesions, cerebral edema, senile dementia, Alzheimer's disease, diabetic neuropathies, etc." (see page 58, lines 2-4), stimulating fibroblasts, megakaryocytes, hematopoietic cells, immune system cells, vascular smooth muscle cells treating bone fractures and osteoporosis, diagnosis and treatment of cerebral tumors (see page 58, lines 11-16). Neither the specification nor the prior art demonstrates a correlation or nexus of the claimed nucleic acid molecule with any of the conditions or disorders contemplated by the instant specification, therefore, there is no evidence of record that would provide for a method of treating/diagnosing any of the listed conditions or disorders. The results presented in the Declaration also fail to establish a use of the claimed nucleic acid in the any of the disclosed methods. Additionally, the fact that the FGF-CX protein induces transformation of fibroblast cells in culture means that the protein could not be used for wound healing.

Contrary to Applicant's assertion, the fact that the disclosed protein induces cell proliferation in NIH 3T3 cells does not establish that the claimed invention is involved in tumorigenesis. A number of different agents may stimulate cell proliferation *in vitro*, but that does not establish a nexus between the agent and cancer without a demonstration that the relationship is also present *in vivo* in a particular cancer. Applicant has provided no evidence linking the claimed invention with any cancer or proliferation-associated disorder.

Applicant argues at pages 5-6 that the claimed invention is a member of the FGF family and that assignment to the FGF family imputes a specific, substantial and credible utility to the instant invention. However, as illustrated by Galzie et al., the FGF family does not share the same specific, substantial and credible utility since they have distinct biological activities which cannot be predicted from their amino acid structure. Applicant asserts that the protein encoded by the claimed DNA is 100% identical to human FGF-20, however, this information was not available at the time of the filing of the instant application and cannot be used as a basis for utility since the biological functions of the claimed invention are not taught in the instant specification.

Applicant argues that the submitted Exhibits demonstrate to one of ordinary skill in the art that the claimed invention could be used as markers for cancer and angiogenesis (see page 6 of the response). This argument is not persuasive since no evidence has been provided that claimed invention is associated with any particular cancer or disorder. The ability of a compound to stimulate a cell in vitro does not establish a nexus between that compound and a disease state. Taken to the extreme, FGF-2 stimulates fibroblasts, but it is clearly not a marker for all cancers or angiogenesis. The instant application fails to provide evidence that the claimed invention is a marker for a disease state, wherein expression is diagnostic for a particular condition based on an increased/decreased expression compared to normal tissue. Therefore, in the absence of a nexus or correlation with a particular disease or cancer, the instant specification does not disclose a credible "real world" use for the claimed invention, it is incomplete and, therefore, does not meet the requirements of 35 U.S.C. §101 as being useful.

Claim Rejections - 35 USC § 112

10. Claims 1-2, 4-5, 7-10, 14, 19-20, 28-29 are rejected under 35 U.S.C. §112, first paragraph, as failing to adequately teach how to use the instant invention for those reasons given above with regard to the rejection of these claims under 35 U.S.C. §101 and for the reasons of record in paper #12.

11. Claims 14 and 29 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claim 14 is directed to a method of producing a polypeptide. However, claim 14 ultimately depends from claim 1, which includes both encoding and complementary nucleic acid molecules. The instant specification fails to teach how to make a polypeptide using the complementary nucleic acid molecule which by definition does not encode the polypeptide, therefore, the claim is not enabled for such material. Applicant argues that claim 14 recites that the FGF-CX polypeptide is defined by the amino acid sequence provided in SEQ ID NO:2. This argument is not persuasive because the method calls for the use of the host cell of claim 10 which contains the DNA of claim 1, which specifically recites coding and non-coding DNA. This rejection could easily be corrected by an intervening claim to the coding strand, or rewriting the method as an independent claim.

12. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

13. Claims 1, 3-4, 19-21, 28 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1 and 28 recite "FGF-CX", however, reference to this term is indefinite as it is not art recognized and it is not clear what limitations this term places on the claimed invention. Applicant asserts that FGF-CX is defined by the sequences in SEQ ID NO:1 and 2. This argument is not persuasive since it is not clear what an "FGF-CX nucleic acid molecule" would be versus any nucleic acid molecule encoding SEQ ID NO:2. Therefore, the metes and bounds of what is considered "FGF-CX" cannot be determined from the claim, and it is indefinite.

Claims 4 and 28 recite "hybridizes .... under stringent conditions", wherein such conditions are not recited in the claim. The metes and bounds of the recitation "hybridizing under stringent conditions" cannot be determined because, depending on the conditions which are used, many different molecules could be intended by the claims. Applicant argues at page 8 of the response that the specification "clearly describes stringent conditions" on page 17 at line 9. However, this is not completely correct. The specification at page 17 provides several definitions for "stringent conditions" and clearly indicates that "[s]tringent conditions are sequence-dependent and will be different in different circumstances" (see line 18-19). Conditions are described, but these appear to be exemplary (see for example page 17, lines 25-30). Page 18 of the specification provides for

a set of conditions for high stringency, but then states that these conditions are non-limiting and that conditions are such that different % identities are intended and other conditions are found in the art. Therefore, based on this disclosure, it is not clear which set of conditions are intended by the claims, and since the specification clearly contemplates a number of different conditions which are all stringent as well as specifically stating that the conditions are "sequence-dependent and will be different in different circumstances", the metes and bounds of the claims cannot be determined.

The inclusion of those conditions which are intended by the recitation of "stringent", or reference to a specific definition in the specification (i.e. not optional conditions, or a range of conditions) would obviate this ground of rejection.

Claim Rejections - 35 USC § 102

14. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

15. Claims 5 and 28-29 are rejected under 35 U.S.C. 102(b) as being anticipated by Nauro et al. (U.S. Pat. No. 5,512,460) for the reasons of record in paper #12.

Applicant argues that the amended claim 5 no requires that "conservative amino acid substitution be made within the context of SEQ ID NO:2, without altering the functional ability of the FGF-CX polypeptide" (see page 8 of the response) and that the claims no longer recite derivative, analog or homolog. This argument is not persuasive because a "conservative"

substitution is one that conserves something, which could be function. Claim 5 states that the "functional ability" of the protein is not altered, but it fails to indicate which functional ability. Claim 28 does not require any conservation of function and claim 29 includes the function of glia activation. Since claim 5 has no upper limit on the number of substitutions which could be made, and conservation could be the function of the protein, the molecule of Nauro et al. appears to meet the limitations of the claims. It is a nucleic acid molecule which encodes a protein which has an activity which is asserted for the disclosed protein. The nucleic acid molecule of Nauro et al. does not encode "FGF-CX" as recited in claim 28, but in light of this term being indefinite for the reasons provided above, the claims are anticipated since all the structural limitations are met, absent evidence to the contrary.

Conclusion

16. No claim is allowed.

17. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Christine J. Saoud, Ph.D., whose telephone number is (703) 305-7519. The Examiner can normally be reached on Monday to Thursday from 8AM to 2PM. If attempts to

reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Gary Kunz, can be reached on (703) 308-4623.

Certain papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1 (CM1). The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. §§ 1.6(d) and 1.8). NOTE: If Applicant *does* submit a paper by fax, the original signed copy should be retained by Applicant or Applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers.

Official papers filed by fax should be directed to (703) 872-9306. If this number is out of service, please call the Group receptionist for an alternate number. Official papers filed After Final rejection filed by fax should be directed to (703) 872-9307.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

CHRISTINE J. SAOUD
PRIMARY EXAMINER

Christine J. Saoud